What is the purpose of this study?

Dense breast tissue is a frequent finding on mammogram that has been shown to be a risk factor that increases the risk for developing breast cancer over time. This research study tests whether putting a clear, odorless gel, which contains an active byproduct of tamoxifen called 4-OHT, on the skin of both breasts daily decreases breast density on mammogram when compared to a placebo gel that does not contain any active medication.

Why a topical gel versus a pill?

The tamoxifen pill has been shown to lower breast cancer risk and to reduce breast density. However, many women don’t take the pill because of concerns about side effects. Recent research shows that when 4-OHT gel is applied directly to the breast, the drug gets into the breast with less drug getting into the blood. This goal of this trial is to find a way to lower the risk of breast cancer with fewer side effects.

Are there risks?

Before you agree to participate in the study, your health care provider will discuss the possible risks of taking part in the trial. This way, you can make sure that participating in the study is the right choice for you. You can withdraw from the study at any time for any reason and continue with your standard care.

Will I benefit from the study?

Taking part in this study may not directly benefit you but your participation will help our teams learn more about topical 4-OHT gel and its potential to reduce breast density.
Who can participate?

Women may participate in the study if they:

- Are not pregnant and are 40-69 years old or under 40 and at higher risk (decided based on a Gail score—a model that predicts risk);
- Have dense breasts on mammogram;
- Are willing to avoid exposing breast skin to natural or artificial (tanning bed) sunlight for the duration of the study (12 months).

If you are eligible and you give consent, you will be randomly assigned to either the topical 4-OHT gel or topical placebo gel group. Neither you nor your study team decides which group you are in.

What does this study involve?

- Your mammogram will be reviewed for breast density eligibility.
- Blood work will be drawn for lab tests and research purposes. If you are still menstruating you will have a pregnancy test.
- If eligible, you will receive pump canisters for easy application of the topical 4-OHT gel or placebo gel and instruction on how to apply the gel daily. You will also receive a daily diary to record each day that you apply the study gel.
- At 6 months, you will return for a breast exam visit, blood work, return your canisters and receive new ones. We will discuss any issues you may or may not be having while on the study.
- At 12 months you will return for your annual mammogram and breast exam. We will collect your canisters, study diary and get bloodwork. We will collect your 24 month mammogram as well.

Optional Breast Biopsy:

You will also be asked if you would be willing to undergo a needle biopsy of your breast at the beginning and end of the study. The biopsies are to test whether the topical gel with the active ingredient, 4-OHT, is more effective than placebo gel in slowing the division of breast cells, or causing the cells to die and disappear, a process that is thought to lower breast cancer risk. These biopsies are optional. Compensation will be provided to cover related expenses.

Where is this study being conducted?

This study is being conducted in conjunction with the National Cancer Institute and four major Cancer Centers:

- Dana-Farber Cancer Institute, Boston MA
- MD Anderson Cancer Center, Houston TX
- Moffitt Cancer Center, Tampa FL
- Northwestern University, Chicago IL